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Systematic review of the association between Alzheimer's disease and chronic glaucoma

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Dear editor

We read with great interest the paper by Tsilis et al entitled "Systematic review of the association between Alzheimer's disease and chronic glaucoma" published recently in this journal.¹ The potential overlap in the pathobiological background of Alzheimer's disease (AD) and primary open angle glaucoma (POAG) is currently a topic of intense discussion and could provide further insight into both of these complex diseases.

Last year, we published an extensive review on POAG and the potential link between AD and POAG.² Both AD and POAG consist of several clinical subtypes, and are genetically heterogeneous disorders. In our POAG disease model, we found that at least 65 candidate disease genes, together defining several molecular mechanisms (developmental dysfunction, lipid metabolism, and inflammatory processes), underlie the disease.² For AD, at least 31 genes have been associated with the disease.³ We also showed that, on a molecular level, there is overlap between the molecular mechanisms of POAG and those of AD.⁴

When comparing two (genetically) heterogeneous disease entities, the conclusion that high heterogeneity and nonassociation will be found seems obvious. The study by Cumurcu et al⁵ cited by Tsilis et al, concerns a very distinct form of glaucoma, ie, pseudoexfoliation glaucoma, caused uniquely by mutations in the *LOXL1* gene,⁶ and AD. We believe that this study should be considered separately, or pooled with data from other pseudoexfoliation glaucoma (and AD) studies. The data from this study cannot be extrapolated to others.

We agree with Tsili et al that large and high-quality association studies, preferably with long follow-up, are needed to clarify the existence and nature of possible associations between POAG and AD. However, at the same time, these studies will only be useful if specific clinical or genetic subtypes of glaucoma and AD are considered. In this respect, we proposed to investigate the existence of a possible association between normal tension glaucoma and AD.²

Disclosure

The authors report no conflicts of interest in this work.

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